

Remarks

Applicants request consideration of the above-referenced patent application.

I. Amendments to Claims

This amendment cancels claim 15. Thus, claims 8-11 and 13 are pending. Claims 8, 11, and 13 are amended. The claims, including the amendments, are shown in the previous section. Applicants submit that the amendments do not introduce new matter. Specifically:

In claim 8, several of the A¹ structures have been amended to correct obvious errors and to more clearly define the substituents.

Claims 11 and 13 have been amended to remove references to tumor metastasis, tumor growth, solid tumor growth, and angiogenesis.

Other amendments rephrase the claims, remove redundancies or unnecessary terms, or correct grammatical or obvious errors. Applicants submit that such amendments are permissible under MPEP §2163.07.

Applicants reserve the right to pursue any canceled subject matter (or any other subject matter disclosed in this application) in one or more later-filed divisional and/or continuation applications.

II. Response to rejection of claims 10, 11, 13, and 15 under 35 U.S.C. §112 (first paragraph) in Section 1 of the Office action

Claims 10, 11, 13, and 15 have been rejected under 35 U.S.C. §112 (first paragraph) for failure to enable their entire scope. Applicants request withdrawal of this rejection.

In order to be enabled under 35 U.S.C. §112, first paragraph, “the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation’.” *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Questions of enablement are evaluated against the claimed subject matter and the first analytical step requires a determination of exactly what subject matter is encompassed by the claims. See MPEP 2164.08. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further, the scope of enablement must only bear a “reasonable correlation” to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

In the instant case, the Office action bases this rejection on common knowledge in the field regarding the large number of diverse types of tumors, on the absence of any generally effective agent for treatment of tumors, and on an article by Reynolds, et al., reporting purported findings of tumorigenesis and tumor growth in the absence of $\alpha_v\beta_3$ and $\alpha_v\beta_5$.

In response to the rejection, Applicants have amended claims 11 and 13 to remove references to tumor metastasis, tumor growth, solid tumor growth, and angiogenesis. Applicants are making this amendment to expedite prosecution of this application, and make no representation as to the merits of the rejection.

Applicants submit that amended claims 11 and 13 are enabled. Applicants' specification provides a detailed background discussion relating to the role of $\alpha_v\beta_3$ and $\alpha_v\beta_5$ with respect to the conditions listed in amended claims 11 and 13. See Applicants' specification at, for example, pages 1-4. Applicants' specification also provides detailed instructions for using the claimed invention to treat these conditions. For instance, the specification provides details regarding assays for analyzing the effectiveness of compounds in inhibiting and antagonizing $\alpha_v\beta_3$ and $\alpha_v\beta_5$. See, e.g., Applicants' specification at page 104, line 1 to page 110, line 4. It also includes discussion relating to pharmaceutical compositions and their use in the claimed methods, including, for example, details relating to examples of contemplated routes of administration for such compositions, examples of contemplated dosages and dosage regimens, examples of various contemplated adjuvants that may be included in such compositions, and examples of additional contemplated active ingredients that may be included in such compositions. See, e.g., Applicants' specification at page 27, line 17 to page 33, line 45. This discussion would enable one skilled in the art to practice the claimed methods of amended claims 11 and 13. Although practicing such methods may, in some instances, require experimentation, such experimentation is the type that one skilled in the art would typically engage in when preparing pharmaceutical compositions. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. See MPEP §2164.01. Thus, Applicants submit that the experimentation in this case is not the type that should be construed as "undue experimentation." Accordingly, Applicants submit that the claims are enabled and request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claim 10 is directed to a pharmaceutical composition comprising a compound, enantiomer, tautomer, racemate, polymorph, or salt of claim 8 in an amount that inhibits or antagonizes $\alpha_v\beta_3$ or $\alpha_v\beta_5$. Applicants submit that this claim is enabled. Applicants have provided assays for analyzing the inhibitory effectiveness of a compound-in-question, as well as data demonstrating the use of those assays with compounds that Applicants have prepared in accordance with this invention. See, e.g., Applicants' specification at page 104, line 1 to page 110, line 4. Applicants have also provided a detailed discussion relating to preparation and use of the claimed pharmaceutical compositions. See, e.g., Applicants' specification at page 27, line 17 to page 33, line 45. This discussion, for example, includes details relating to examples of contemplated routes of administration for such compositions, examples of contemplated dosages and dosage regimens for such compositions, examples of various contemplated adjuvants that may be included in such compositions, and examples of additional contemplated active ingredients that may be included in such compositions. One skilled in the art would be able to use this discussion to prepare the compositions recited in claim 10. Although such preparation may, in some instances, require some experimentation, one skilled in the art would typically engage in such experimentation when preparing a pharmaceutical composition. As noted above, such experimentation is not the type that should be construed as "undue experimentation." Thus, claim 10 is enabled.

Claim 15 has been canceled, thereby mooting the objection as to this claim.

III. Response to rejection of claims 10, 11, 13, and 15 under 35 U.S.C. §112 (second paragraph) in Section 2(g) of the Office action

Claims 10, 11, 13, and 15 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully request withdrawal of this rejection.

The Office action indicates that the terms "tumor metastasis," "tumor growth," "solid tumor growth," and "neoplasia" are indefinite. In order to expedite prosecution, claims 11 and 13 have been amended to remove the terms "tumor metastasis", "tumor growth", and "solid tumor growth." Claim 15 has been canceled, thereby mooting the objection as to the term

“neoplasia.” Thus, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

IV. Response to double-patenting rejection of claims 8-11, 13, and 15 in Section 4 of the Office action

Claims 8-11, 13, and 15 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over the claims of U.S. Application No. 10/363,070. Because the claims of U.S. Application No. 10/363,070 and the instant application have not yet been found to be otherwise allowable, Applicants submit that this rejection must remain provisional. Applicants will address this issue (to the extent necessary) once the claims have been found to be otherwise allowable.

V. Response to rejection of claims 8, 10, 11, 13, and 15 under 35 U.S.C. §112, first paragraph in Section 8 of the Office action

Claims 8, 10, 11, 13, and 15 have been rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement with regard to the definition of A¹ in claim 8 as amended by Applicants’ Amendment C. Applicants request withdrawal of these rejections.

- a) Applicants submit that the structures at issue are supported by Applicants’ specification at, for example, page 15, line 1 (see last structure in that line); and claim 8 (as originally filed), at the top of page 120. Specifically, original claim 8 defines R as hydrogen or methyl such that 3-amino-isoquinolin-1-yl and 3-methylamino-isoquinolin-1-yl are disclosed in the specification.
- b) Applicants submit that the structures at issue are supported by Applicants’ specification at, for example, page 12, line 3 (see second structure in that line) and page 14, line 2 (see third structure in that line). Although claim 8 (as originally filed) and Applicants’ specification at page 15, line 2 (first structure in that line) define “B” as N or CH, this is an obvious typographical error, as evidenced by the corresponding

definitions on pages 12 and 14 and by the fact that the "B" position is a divalent position (NH, O, and S are all divalent, whereas N and CH are trivalent).

- c) The structures at issue have been canceled from claim 8, thus obviating the rejection in section 8(c) of the Office action.
- d) The structures at issue have all been amended to replace the nitrogen atom that was inadvertently deleted by Applicants' Amendment B from the heterocycle ring of the structure corresponding to the structures at issue. The amended structures are supported by Applicants' specification at, for example, page 15, line 3 (see last structure in that line); and claim 8 (as originally filed), at page 120, line 3 (see last structure in that line).

Claims 10, 11, and 13, which depend from claim 8, are submitted as patentable under 35 U.S.C. §112, first paragraph, for at least the same reasons as claim 8. Claim 15 has been canceled, thereby mooting the rejection as to that claim.

VI. Response to rejection of claims 8, 10, 11, 13, and 15 under 35 U.S.C. §112, second paragraph in Section 9 of the Office action

Claims 8, 10, 11, 13, and 15 have been rejected under 35 U.S.C. §112, second paragraph for reciting a structure that contains a nitrogen atom that is not valence satisfied. Applicants request withdrawal of this rejection.

The structure at issue in claim 8 has been amended to add a hydrogen atom to the nitrogen atom that was not valence satisfied. This amendment is supported by Applicants' specification at, for example, page 15, line 2 (see last structure in that line); and claim 8 (as originally filed), at page 120, line 2 (see last structure in that line). Applicants submit that this amendment overcomes the rejection in Section 9 of the Office action.

Claims 10, 11, and 13, which depend from claim 8, are submitted as patentable under 35 U.S.C. §112, second paragraph, for at least the same reasons as claim 8. Claim 15 has been canceled, thereby mooting the objection as to that claim.

VII. Response to the objection to claim 9 in Section 10 of the Office action

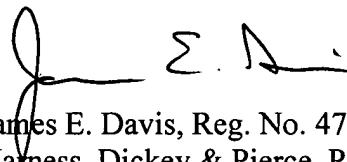
Claim 9 has been objected to for depending from a rejected claim (*i.e.*, claim 8). Applicants believe that amended claim 8 is patentable such that claim 9 is a proper dependent claim. Applicants respectfully request that the objection be withdrawn.

* * * * *

Enclosed is a check in the amount of \$1,020.00 for the purchase of a three-month extension of time under 37 C.F.R. §1.136(a). Applicants believe that they do not owe any other fees in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **08-0750**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

Applicants submit that the pending claims are in condition for allowance, and request that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,

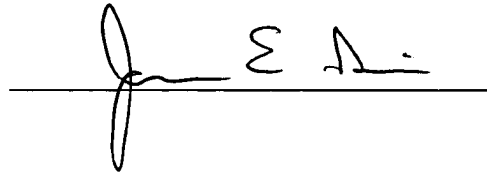


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Amendment D
U.S. Appl. 09/942,174
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CERTIFICATE OF MAILING UNDER 37 CFR § 1.8

I certify that this correspondence is being deposited with the U.S. Postal Service on **October 20, 2005** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.**

A handwritten signature in black ink, appearing to be "J. E. D.", is written over a horizontal line.

JED/LMR/PML